

## Possible Allergic-Rhinitis-Inducing Effects of Volatiles in Perfume

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### Introduction

Chemical analysis has shown that about 2500 kinds of fragrance ingredients are currently used in cosmetic products, and common allergens are generally used in 15-100% of cosmetic products. In some cases, even a combination of three or four allergens exists in one single product. According to reports, at least 100 of those ingredients are known allergens. Thus, it is impossible to avoid exposure in our daily life<sup>[1]</sup>. Perfume exposure may cause respiratory symptoms. Allergic rhinitis is a worldwide health problem, 10-25% of the world population more or less suffered from it, which could lead to many social problems such as loss of the labour force.

Some fragrances are known to be significant skin and potential airway sensitizers<sup>[2]</sup>.

Allergic rhinitis usually happens to specific individuals after their contacting with allergens, mostly mediated by IgE (especially histamines) and participated by many immune-active cells and cytokines. It is a non-infectious inflammatory disease of the nasal mucosa. Traditionally, common pathogens include genetic factors, mite, pollen, animal slander, and fungus. Inhalation of allergens is the main pathogenesis route of allergic rhinitis, which can last for at least 1 hour a day for many days during the year<sup>[1, 2]</sup>.

With the exposure of cosmetic and perfume in our daily life, current research indicates that some ingredients are involved in affecting human health, this article focus on perfume-related allergic rhinitis. From the beginning, some common symptoms and the pathological mechanism of allergic rhinitis has been introduced, therefore, it is necessary to discuss some potential sensitizing ingredients in the perfume. Although it is undoubted that perfume has some certain correlation with allergic rhinitis, due to the complicated constitution, the difficulty of determination is extreme. As a result, no powerful statistic and efficient experiment evidence has been discovered in this field.

### Allergic Rhinitis

Three necessary conditions mediate the initiation of allergic rhinitis: specific antigen, specific individual, and specific antigen encounter with specific individual.

According to Durham et al., ID4 is secreted by activated Th2 lymphocytes. It has the function of stimulating B lymphocytes to produce IgE, which combines Fc fragment with the receptor of mast cell. In terms of allergic response, pre-formed mediators are released by the allergen, and histamine is an indispensable mediator during the process. Furthermore, the HI receptors affects its surrounding microenvironment, which can lead to histamine-dependent manifestations like nasal itching, sneezing, nasal congestion, and serous rhinorrhoea<sup>[3]</sup>.

### Perfume allergy

A dose-dependent sensitization response for each allergen has been reported. When the allergens were mixed, an increased response was shown. In terms of the test results, mixtures of allergens enhance the primary response that potentiates the generation of memory T cells in answer to specific allergen<sup>[4]</sup>.

### Cellular Infiltration of allergic rhinitis

A variety of mediators are responsible for the edema of the nasal mucosa, including the products of cell membrane phospholipid conversion (LTB<sub>4</sub>, LTC<sub>4</sub>, PGT<sub>2</sub>, eicosatetraenoic acid, and PAF) and neuro modulators (substance R), all these factors lead to the symptoms of allergic rhinitis, such as vasodilatation, transudation and edema. Eosinophils dominate the subsequent process of the allergic response, which affects the response via releasing cytotoxic proteins, lipid mediators, oxidative radicals, and cytokines. Among these, IL-3, IL-5, and IL-8 contribute to the maturation and differentiation of the eosinophils<sup>[3]</sup>. Multiple mediators which are released from eosinophils, such as the platelet-activating factor (PAF) and leukotrienes expand the capacitance vessels and induce exudation of plasma

components from post capillary venues, as a consequence of nasal mucosa swelling. On the other hand, PAF accelerates the histamine-induced swelling of the nasal mucosa, while leukotriene (LT), D4, and ECP boost the histamine-mediated secretion of nasal effusion<sup>[5]</sup>. Additionally, Th2 cells play a significant role in allergic mucosal inflammation, which could lengthen the allergic response. Three crucial endothelial adhesion molecules include intercellular adhesion molecule-1 (ICAM-1), VCAM-1, and E-selectin. IL-1, tumor necrosis factor (TNF), and lipopolysaccharide can inhibit these molecules on endothelial cells<sup>[6]</sup>.

### Nervous domination of allergic rhinitis

Sympathetic, parasympathetic and peripheral sensory nerves may participate in allergic rhinitis. Neuropeptide Y is a type of neither vasoconstrictor, which co-localizes with nor epinephrine in sympathetic fibers. Neuropeptide Y not only induces vasoconstriction but also strengthens the expression of intercellular adhesion molecules<sup>[6]</sup>. Olfactory receptor (or) and the olfactory cells of human olfactory receptor locates in the top side of the nasal cavity. As a type of G-protein-coupled receptor, OR recognizes scent by activating the signal transduction pathway and detecting the odorant molecules present in the surrounding environment. These receptors build up the biggest transmembrane protein family in the human genome<sup>[7]</sup>. In the process of the human olfactory response, olfactory cells and environmental substance is received and conducted by olfactory cells, and olfactory bulb (olfactory nerve) processes olfactory information, which brings sensations to the brain.

### Perfume-related allergic rhinitis

Perfumes provide attractive scents to make the products more popular, owing to they are mixtures of dozens of complicated substances and natural extracts<sup>[8]</sup>. Perfumes have been proved to contain allergens of allergic rhinitis. Some volatile components of perfume can stay on the surface of clothes and skin for a long period. Therefore, if allergic rhinitis patients are allergic to any kind of ingredient, a series of allergic symptom would appear. The exposure may cause respiratory symptoms such as discomfort, difficult, or labored breathing, and coughs. The majority of symptoms are slight, but the outcomes can be serious and even affect daily activities. Possible explanations for the co-occurrence of perfume-related respiratory symptoms in HE, CA, and asthma includes genetic factors, environmental factors, physiological factors associated with inflammation, and increased general tendency to report symptoms. However, the current evidence indicates that inhalation exposure to fragrance materials in skin sensitized individuals does not cause allergic reactions in the respiratory tract<sup>[9]</sup>. Nevertheless, Elberling proposed that perfume induced a dose-dependent non-IgE mediated release of histamine from peripheral blood basophils, enhance basophil reactivity to perfume was detected in patients with respiratory symptoms<sup>[10]</sup>. Hence, the mechanism is still a controversial topic, so there is a demand that more research should explore the connection between perfume and allergic respiratory diseases, especially allergic rhinitis, which has few relevant statistics or experimental results.

### Respiratory allergy and allergy contact dermatitis (ACD)

Respiratory symptoms which are related to fragrance co-occur Among the patients with asthma, contact dermatitis and/or atopic dermatitis, however, the pathophysiological mechanisms are unexplained, it is required to use antihistamine, but no efficient treatments aimed at these symptoms have yet been applied<sup>[11]</sup>. Respiratory allergy is a type I hypersensitivity of the upper and lower respiratory tract to an allergen, which is mediated by IgE. by contrast, ACD is a type IV hypersensitivity which is mediated by T cells<sup>[12]</sup>. However, it has not been proved that allergic symptoms induced by inhalation exposure or ACD, since skin exposure to allergy also can stimulate immune response when with such allergens can stimulate the quality of immune response required for effective sensitization of the airways, as a consequence, It is inaccurate to take inhalation expose into consideration merely since skin exposure also could induced respiratory allergic response, although it is undoubted that sensitization can be induced in this way, the partial skin exposure to respiratory allergens can also lead to sensitization of the respiratory tract, that is to say that skin contact with such allergens can stimulate the quality of immune response needed for efficient sensitization of the airways. Therefore, when exploring the potential risks of fragrance to induce the respiratory allergic reaction, it is necessary to analyze the two routes both. Until now, few reports has been proved whether perfume ingredients have any potential to induce sensitization of the respiratory tract directly<sup>[9]</sup>.

Inhalation of high concentrations of fragrance contact allergens pose a threat to some haematogenic contact dermatitis patients, nevertheless, the changes of the respiratory tract are limited to symptoms in some subjects, which had no objective changes<sup>[2]</sup>.

### Knowledge gap

Until now, the pathophysiology of perfume-related respiratory symptoms is indistinctive. Owing to its multiple chemical sensitivity, it is still a complex problem with unclear etiology<sup>[13]</sup>. As a result, few studies indicated the exact connection between perfume, allergic rhinitis, and the olfactory receptor. Additionally, which ingredients are responsible for the allergic response is still understudied. Potential sensitized ingredients include lemon extract, flavouring rose essence, especially Loral Chloroatranol, Atranol, HICC and oak moss had already been forbidden to use in perfume production. Without a doubt, the safety of perfume ingredients is the first critical factor for the cosmetics industry; the perfume manufacturers have the responsibility to handle stricter and safer production technology to meet the increasing needs of public. More studies should as well focus on the analysis of separated ingredients with high-risk of respiratory sensitization. In conclusion, further research needs to focus on investigating the gaps between perfume and allergic rhinitis.

**Conflict of interest:** The authors declare no conflict of interest.

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